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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,922	01/30/2006	Philip John Hogg	05-363	1798

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EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,922	HOGG, PHILIP JOHN	
	Examiner	Art Unit	
	CRAIG RICCI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *6-8 and 24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 9-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/23/2009 and 4/24/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/23/2009 has been entered.

Status of the Claims

2. The amendments filed 3/23/2009 and 4/23/2009 were entered.

Response to Arguments

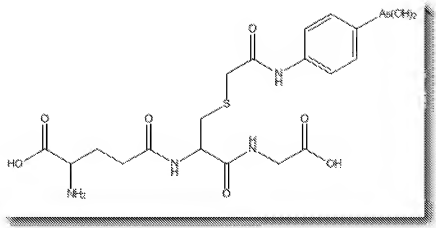
3. Applicants' arguments, filed 3/23/2009 and 4/23/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. **Claims 1-5 and 9-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Constantini et al* (cited in a previous Action), *Sawada et al* (cited in a previous Action), and *Hogg et al* (cited in a previous Action).**

6. Instant claims 1-5 are drawn to a process for identifying a compound (or compounds) which selectively induces the mitochondrial permeability transition (MPT) in proliferating cells compared to non-proliferating cells or growth quiescent cells, wherein said method comprises (A) contacting a proliferating cell or cell extract with a compound (or compounds); (B) contacting a non-proliferating cell or growth quiescent cell with said compound (or compounds); (C) determining whether the compound (or compounds) binds to the ANT; and (D) determining whether said ANT-binding compound selectively induces the MPT in proliferating cells compared to non-proliferating or growth quiescent cells by measuring cytochrome c release and changes in cellular superoxide concentration. More specifically, as elected by Applicant, the compound to be tested is 

.

The process, as summarized above, reads on claims 1-5 and 9-23.

7. As discussed in the previous Action, *Constantini et al* teach that agents which bind ANT induce MPT and cause apoptosis (Abstract; Page 307, Column 2; and Page 311, Column 2).

Specifically, *Constantini et al* state that "our data suggest that ANT may be (one of) the critical target molecule(s) responsible for mitochondrial membrane permeabilization and cell death" (Page 311, Column 2). Since "[f]ailure to undergo apoptosis is one of the mechanisms of oncogenesis and/or chemoresistance of transformed cells" (Page 307, Column 1) and since "[m]itochondrial membrane permeabilization is a critical event in the process leading to physiological or chemotherapy-induced apoptosis" (Abstract) the skilled artisan would have found it *prima facie* obvious that agents which bind ANT, induce MPT, and cause apoptosis could be used as chemotherapeutics in the treatment of cancer, with a reasonable expectation of success. Indeed, *Constantini et al* explicitly motivate the design of such drugs (Page 312, Column 1). However, as noted by *Sawada et al*, "[o]ne of the major problems in human cancer chemotherapy is the nonspecific action of antitumor agents, which can cause unwanted damage to normal [growth quiescent] cells" (Column 1, Lines 19-21). Accordingly, in further view of *Sawada et al*, the skilled artisan would have found it *prima facie* obvious that agents which ***selectively*** bind ANT, induce MPT, and cause apoptosis in proliferating cells (compared to non-proliferating or growth quiescent cells) would be ***especially*** useful chemotherapeutics in the treatment of cancer (compared to agents which are nonselective) since such selective agents would not result in unwanted damage to normal (growth quiescent) cells. Thus, in the treatment of cancer, the skilled clinician would have found it *prima facie* obvious to administer - to a patient in need of cancer treatment - chemotherapeutic agents which **(1)** bind ANT, induce MPT, and cause apoptosis (in view of *Constantini et al*) and **(2)** which do so selectively in proliferating cells (in view of *Sawada et al*), in order to provide effective chemotherapeutic agents which do

not result in unwanted damage to normal (growth quiescent) cells, with a reasonable expectation of success.

8. Chemotherapeutic agents which are useful for the treatment of cancer are well known in the art. In particular, *Hogg et al* teach that the elected compound is useful in the treatment of proliferative diseases, including cancer (compound of formula IV where -As=O is replaced by the arsenoxide equivalent, $-As(OH)_2$; Page 10, Lines 18-19; Page 12, Lines 8-10; Page 13, Lines 29-30; and claims 40-42). However, *Hogg et al* do not specify whether the compound binds ANT, induces MPT, and causes apoptosis ***selectively*** in proliferating cells. Accordingly, it would have been *prima facie* obvious to determine whether the elected compound species (taught by *Hogg et al*) binds ANT, induces MPT, and causes apoptosis ***selectively*** in proliferating cells in order to assess whether the compound would be an especially useful chemotherapeutic in the treatment of cancer, with a reasonable expectation of success. Thus, to evaluate whether the compound species binds ANT, induces MPT, and causes apoptosis ***selectively*** in proliferating cells (compared to non-proliferating cells), it would have been *prima facie* obvious to contact a proliferating cell or cell extract (as well as a non-proliferating cell or growth quiescent cell) with the compound species and monitor each group (i.e., the cancer group (proliferating cell group) and the non-cancer group (non-proliferating cell group)) for ANT binding and MPT. As disclosed by *Constantini et al*, permeabilization of the mitochondria (MPT) is associated with cytochrome c release (Page 301, Column 2). And, as disclosed by *Cai et al*, permeabilization of the mitochondria (MPT) is also associated with an increase in cellular superoxide (Abstract). Accordingly, in determining whether the instant compound species selectively binds ANT and induces MPT, it would have been *prima facie* obvious to measure changes in cytochrome c

release and changes in cellular superoxide concentration in the two groups (i.e., the cancer group (proliferating cell group) and the non-cancer group (non-proliferating cell group)) following exposure to the compound species, and to compare the findings between the two groups.

9. Thus, for all of the foregoing reasons, instant claims 1-5 and 9-23 are rejected as *prima facie* obvious.

10. Applicants, however, argue that "the results of the presently claimed method could not have been predictable nor would one of ordinary skill in the art have a reasonable expectation of success at the time the present invention was made because it was unknown at the time that MPT could be selectively induced in proliferating cells compared to non-proliferating or growth quiescent cells" (Applicant Argument, Page 18). Yet, as previously discussed, the claims do **not** require that a compound actually induce MPT in proliferating cells and not non-proliferating cells. Applicants' amendments to the claims have not changed this fact. The claims are still drawn to a method of determining ***whether*** a compound binds to ANT and ***whether*** the compound selectively induces the MPT in proliferating cells compared to non-proliferating cells. And, as discussed above, the skilled artisan would have been motivated to determine whether any anticancer chemotherapeutic compound (including the elected compound as taught by *Hogg et al*) binds to ANT and whether said compound selectively induces the MPT in proliferating cells compared to non-proliferating cells ***in order to determine*** whether said agent would be an ***especially*** useful chemotherapeutic in the treatment of cancer. Whether or not the skilled artisan would have expected the compound to selectively induce the MPT in proliferating cells compared to non-proliferating cells is irrelevant since the claims do not require this outcome. That is, the instant claims are merely drawn to an assay for testing whether compounds

selectively induce the MPT. And, as previously discussed, the ordinarily skilled artisan would have been motivated to test whether the elected compound, an anticancer agent, selectively induces the MPT since, **IF** it does, then the skilled artisan would have reasonably predicted that the compound would be ***especially*** useful for the treatment of cancer.

11. Accordingly, Applicants' arguments are not found persuasive.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614